FIG. 1

$$\begin{matrix} & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ \end{matrix}$$

		·		T.cruzi	
Cmpd#	R1	R2	Cruzain IC50 (µM)	Survival (days @ 5µM)	Host Toxicity
1a	2'-phenyl	NH ₂	>20	5 days	none
1b	3'-phenyl	NH ₂	8	43 days	none
1c	4'-phenyl	NH ₂	5	8 days	toxic
2a	2'-NH-phenyl	NH ₂	>20	5 days	none
2b	3'-NH-phenyl	NH ₂	>20	43 days	none
2c	4'-NH-phenyl	NH ₂	>20	43 days	none
2d	3'-O-phenyl	NH ₂	10	27 days	toxic
2e	4'-O-phenyl	NH ₂	10	28 days	toxic
3d	3'-Br	NH ₂	0.06	43 days	none
3e	3'NH ₂	NH_2	>20	5 days	none
3f	2'-OH	NH_2	>20	5 days	none
3 g	3'-OH	NH ₂	>20	5 days	none
3h	4'-OH	SMe	>20	5 days	none
4a	3'-Br	Shit	>20	7 days	toxic
4c	3'-Br	piperidyl	5	5 days	none
4d	3'-Br	N-methylpiperazinyl	5	14 days	toxic
4e	3'-Br	NEt ₂	5	5 days	none

FIG. 2

							•	T.cruzi	
							Cruzain	Survival	
Cmpd#_	R	RI	R2	X	Y	Z	IC50(μM)	(days @5μM)	Host Toxicity
3a	Н	H	NH ₂	N	CH	CH	>20	43 days	none
3b	H	Н	NH_2	CH	N	CH	>20	5 days	none
3c	H	H	NH ₂	CH	CH	N	>20	5 days	none
4b	H	Н	SMe	N	CH	CH	>20	5 days	none
3i	CH(Me)NNHC(S)NH ₂	H	NH_2	CH	CH	CH	5	5 days	none
3j	CH(Me)NNHC(S)NH2	H	NH,	N	CH	CH	>20	5 days	none
3k	CH(Me)NNHC(S)NH2	Me	NH ₂	CH	СМе	N	>20	5 days	none

FIG. 3

Cmpd#	RI	R2	Rhodesain IC50(μM)	T.brucei ED50 (μΜ)
la	2'-phenyl	NH ₂	>20	>20
1b	3'-phenyl	NH_2	1.1	12
1c	4'-phenyl	NH_2	0.09	10
2a	2'-NH-phenyl	NH ₂	>20	>20
2b	3'-NH-phenyl	NH ₂	0.8	8
2c	4'-NH-phenyl	NH_2	18	4.5
2d	3'-O-phenyl	NH_2	0.55	6
2e	4'-O-phenyl	NH_2	8	3
3d	3'-Br	NH_2	0.05	>20
3e	$3'NH_2$	NH_2	>20	>20
3f	2'-OH	NH_2	>20	>20
3g	3'-OH	NH_2	>20	>20
3h	4'-OH	NH_2	>20	>20
4a	3'-Br	SMe	>20	10
4c	3'-Br	piperidyl	4	3
4d	3'-Br	N-methylpiperazinyl	4	2
4e	3'-Br	NEt ₂	1.8	3

FIG. 4

Cmpd#	R	R1	R2 X	Y	z		T.brucei ED50 (µM)
3a	Н	H	NH ₂ N	CH	CH	>20	4
3b	H	H	NH ₂ CH	N	\mathbf{CH}	>20	>20
3с	H	H	NH ₂ CH	CH	N	>20	>20
4b	Н	H	SMeN	CH	CH	>20	0.3
3i	CH(Me)NNHC(S)	H	NH, CH	CH	\mathbf{CH}	0.33	>20
4b 3i 3j	CH(Me)NNHC(S)	H	NH_2N	CH	CH	>20	>20
3k	CH(Me)NNHC(S) NH ₂	Me	NH ₂ CH	CM	eΝ	>20	>20

FIG. 5

$$R_1$$

Cmpd#	R1	R2	Falcipain 2 IC50(μM)	P.falciparum ED50(μM)
1a	2'-phenyl	NH ₂	>20	>20
1 b	3'-phenyl	NH ₂	>20	>20
1c	4'-phenyt	NH ₂	10	>20
2a	2'-NH-phenyl	NF ₂	>20	>20
2 b	3'-NH-phenyl	NH_2	>20	>20
2c	4'-NH-phenyl	NH ₂	>20	9.9
2d	3'-O-phenyl	Nm_2	>20	>20
2e	4'-O-phenyl	NH ₂	>20	>20
3d	3'-Br	NH ₂	>20	>20
3e	3'NM ₂	NH ₂	>20	>20
,3f	2'-OH	NH ₂	>20	>20
3g	3' -OH	NH ₂	>20	>20
3h	4'-OH	NH ₂	>20	>20
4a	3'-Br	SMe	>20	>20
4c	3'-Br	piperidyl	>20	20
4d	3'-Br	N-methylpiperazinyl	>20	4
4e	3'-Br	NEt ₂	>20	>20

FIG. 6

$$\bigcap_{R}^{R_1} \bigvee_{N} \bigcap_{S}^{H_2}$$

Cmpd	# R	R1 R	2 X Y	Z		P. falciparum ED50(um)
3a	Н	·H NH	N CH	CH		0.08
3ъ	H	H. NH	₂ CHN	CH	>20	>20
3с	H	H NH	CHCH	N	>20	>20
4b	H		e N CH			0.03
31	CH(Me)NNHC(S)	√H2H NH	2 CHCH	\mathbf{CH}	>20	>20
3j	CH(Me)NNHC(S)1	√H2K NH	N CH	\mathbf{CH}	>20	0.03
3k	CH(Me)NNHC(S)N	NH ₂ Me NH	2 CHCM	eΝ	>20	>20

FIG. 7

Compound 3a	Structure	Surviv 5 mgs/kg weight	al (toxicity) 20mgs/kg weight
Ja .	N NH2	20 hours (*)	62 hours (**)
4b	The second secon	62 hours (No)	62 hours (No)
3j	NH Ni+2	62 hours (No)	62 hours (No)
2c	NH ₂ HN NH ₂ NH ₂	62 hours (No)	62 hours (No)
4d		62 hours (No)	62 hours (No)
1b	Br NH₂	62 hours (No)	62 hours (No)

^{*}Animal suffered toxic shock after injection, characterization by tremor, loss of mobility, malaise, and death

^{**}Animal survived treatment with malaise, loss of mobility and ruffled hair after injection

FIG. 8

	Γ	T	1
Structure	Cruzain IC50 (µM)	Rhodesain IC50 (µM)	P. falciparum W2 IC50 (μM)
N _N NH ₂	1.5	0.4	>20
H SCH ³	>10	>10	>20
NO S	>10	9	>20
N N N N N N N N N N N N N N N N N N N	0.312	5	>20
T S S S S S S S S S S S S S S S S S S S	>10	not determined (ND)	>20
Safe Safe	>10	>10	>20
	>10	>10	>20
N-N-N-N-N-N-N-N-N-N-N-N-N-N-N-N-N-N-N-	>10	>10	3.3
N N N N N N N N N N N N N N N N N N N	>10	5	>20
Chynh H H H	>10	>10	7.7

Structure	Cruzain IC50 (µМ)	Rhodesain IC50. (μΜ)	P. falciparum W2 IC50 (μM)
NN NH₂	>10	>10	>20
My NAF	>10	>10	>20
- CYNN NH NH	>10	>10	>20
S N N N N N N N N N N N N N N N N N N N	5	0.8	2.5
HN N N N N N N N N N N N N N N N N N N	>10	ND	>20
	>10	>10	0.489
NH CI	>10	>10	0.125
NH CI	>10	>10	0.227
	>10	>10	0.961

Structure	Cruzain IC50 (µM)	Rhodesain IC50 (µM)	P. falciparum W2 IC50 (µM)
The state of the s	>10	>10	0.908
	>10	>10	0.794
S NH N NH N	2	4	0.051
NH NH2	ND	ND	0.242
THE	>10	8	0.957
	ND	4	1.193
	ND	3	1.809
	ND	1	1.226

Structure	Cruzain IC50 (µM)	Rhodesain IC50 (µM)	P. falciparum W2 IC50 (μΜ)
	ND	5	0.833
N-10H	ND	ND	>20
1 N-12 N-10 N-10 N-10 N-10 N-10 N-10 N-10 N-10	ND	ND	>20
3 NH2 N-10H2	ND	ND	>20
N-101-2	ND	ND	>20
N-NH ₂	ND	ND	>20
N-NH N-NH N-NH	ND	ND	>20
	ND	4	0.025

·:

Structure	Cruzain IC50 (µM)	Rhodesain IC50 (μΜ)	P. falciparum W2 IC50 (μΜ)
	1.8	0.11	0.008
	1.6	4	0.028
	ND	ND	0.013
	ND	0.7	0.013
	ND	ND	0.212
	ND	1.8	0.26
	ND	0.42	0.212
	ND	ND	0.19
H'N H N H NH	ND	4	6.521
HN H N N N N N N N N N N N N N N N N N	ND	5.5	0.14

Structure	Cruzain IC50 (µM)	Rhodesain IC50 (µM)	P. falciparum W2 IC50 (μM)
	>10	ND	0.032
S N N N N S	1.5	0.3	1.677
	0.8	0.4	0.054
Fe N-NH S	8.5	ND	>20
Fe N-NH H ₂ N	ND	ND	>20
SHN-N Fe N-NH H ₂ N	3.5	4.2	>20
OHN-N Fe N-NH H ₂ N	ND	ND	>20
SHN-N Fe N-NH SH2N	2	1.8	>20

Structure	Cruzain IC50 (µM)	Rhodesain IC50 (μΜ)	P. falciparum W2 IC50 (μΜ)
HN-N Fe N-NH N-NH H ₂ N	ND	ND	>20
Fe N-NH S	>10	10	>20
Fe N-NH O	ND	ND	>20
Fe N N N N N N N N N N N N N N N N N N N	ND	ND	0.0246
Fe HN N-N N=	ND	ND .	0.0161
HO S NH2 OH H	9	4	>20
HO N.N. NH ₂	2.1	2	>20
HO N S NH2	5	3	>20

Structure	Cruzain IC50 (µM)	Rhodesain IC50 (µM)	P. falciparum W2 IC50 (μΜ)
ON N N NH2	20	10	>20
HO N N NH2	ND	7	>20
CI HO N N N NH ₂	ND	1	0.376
CI HO NOH NH ₂	ND	>10	0.246
HO OH N.N. NH ₂	ND	ND	>20
HO N'N'S	ND .	ND	>20
THO CH H H NH CI	ND	5	0.437
CN OH H H NH NH NH	2.8	2.5	1.065

Structure	Cruzain IC50 (µM)	Rhodesain IC50 (µM)	P. falciparum W2 IC50 (μM)
HO OH H H NH NH	1.8	1.8	0.265
HO OH H H	>10	>10	0.113
HO OH H H NH	ND	ND	0.376
HO NO NH H H	3.5	ND	0.077

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Therapeutic	Index	-	200	-	9643	526
Cytotoxicity	ED _{so} µg/ml	0.04	0.3	8:	13.5	10
	repeat	0.0384 ±	0.0015± 0.0005	0.265 ± 0.66	0.0014 ± 0.0005	0.019 ± 0.009
EDso µg/ml	+/- 95% CL	<1.11 @	61.11 ®	1.1. ®	<1.11 ®	<1.11 ®
	1.	29.66	99.73	98.51	98.45	99.39
% inhibition T. brucei	3	29.66	99.68	100	99.95	99.52
% inhi T. br	10	98.85	99.22	100	100	99.54
	30	98.24	98.76	97.78	100	99.72
Compound	QI .	MC 156	MC 158	MC 159	MC 162	MC 164
Compound Structure		6. N. 2. N. 3. 3. 3. 3. 3. 3. 3. 3. 3. 3. 3. 3. 3.	S N N N	N N N N N N N N N N N N N N N N N N N	S N H H H	N N N N N N N N N N N N N N N N N N N

Therapeutic	Index	ı	8	0	57	20222	159
Cytotoxicity	ED _{so} µg/ml	>300	>300	0.57	3.08	18.2	2.9
	repeat		0.552 ± 0.156	1.331 ± 0.045	0.0537 ± 0.004	0.0009 ± 0.0005	0.0182 ± 0.0012
EDso µg/ml	+/- 95% CL	>30	<1.11 ®	<1.11 @	<1.11 ®		<1.11 ®
	-	7.3	94.85	82.42	99.78	98.74	98.73
% inhibition T. brucei	3	10.09	99.23	98.27	99.92	98.46	99.74
% inhi T. br	10	12.89	60.66	99.25	99.87	98.31	99.76
	30	15.25	99.84	99.23	100	97.82	99.44
Compound	QI	MC 172	MC 172B	MC 176	MC 177	MC 184	MC 186
Compound Structure		H ₂ N H ₂ N N H ₂	HZHN H N N N HZH	H. H. N. N. N. S.	SH NH		Mes H N N SMe